REMARKS

Upon entry of this amendment, claims 1 and 4 will be amended, and claims 22 and 23 will be added, whereby claims 1-23 will be pending. Claim 1 is the sole independent claim.

Applicant respectfully submits that the amendments to claims 1 and 4 are cosmetic in nature, should not be considered to be narrowing amendments, and no estoppel should be deemed to be associated therewith.

Claims 22 and 23 have been added to further define Applicant's invention. In particular, claim 22 further defines the invention recited in claim 1 by indicating that the adhesion site-controlling layer is attached to the protecting layer. Moreover, claim 23 further defines the invention recited in claim 1 by indicating that the drug-carrying layer is sealed between the adhesion site-controlling layer and the protecting layer to prevent leaking of the drug, such as disclosed at the bottom of page 13 through the top of page 14 of Applicant's specification.

Reconsideration and allowance of the application are respectfully requested.

Response To Formal Matters

Applicant expresses appreciation for the acknowledgment of the claim of priority under 35 U.S.C. 119 as well as receipt of all of the certified copies in this national stage application.

Applicant also expresses appreciation for the inclusion in the Office Action of the initialed copy of the Form PTO-1449 submitted with the Information Disclosure Statement filed October 2, 2001, whereby the Examiner's consideration of the disclosure statement is of record.

Applicant is submitting on even date herewith a Supplemental Information Disclosure Statement. The Examiner is respectfully requested to indicate consideration of the Supplemental

Information Disclosure Statement by forwarding an initialed copy of the Form PTO-1449 submitted therewith with the next communication from the Patent and Trademark Office.

Response To 35 U.S.C. 103(a) Rejections

The claims are rejected in the following rejections:

Claims 1-10 and 12-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Takayanagi et al., U.S. Patent No. 4,765,983, in combination with Caldwell et al., U.S. Patent No. 4,767,627.

Claim 11 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Takayanagi, U.S. Patent No. 4,765,983, in combination with Caldwell, U.S. Patent No. 4,767,627, further combination with Uyama et al., U.S. Patent No. 6,086,869.

In the rejection of claims 1-10 and 12-21, the rejection initially indicates what is considered to be disclosed in each of Takayanagi and Caldwell. The rejection further notes that Takayanagi does not expressly teach that the film is contained in a capsule. Thereafter, it is concluded that it would have been obvious to a person of ordinary skill in the art to prepare a film or tape comprising an active agent in a matrix of polymers and to place that tape or film in a capsule for oral administration. It is contended (referring to Caldwell, column 3, lines 3-11) that one having ordinary skill in the art would have been motivated to do this to retain a dosage form in the stomach for an extended period of time thereby improving bioavailability of the drug.

In the rejection of claim 11, it is contended that it would have been obvious to place an active agent, such as interferon, in a film composition that is administered in a capsule form, apparently based upon the disclosure of Uyama.

Applicant respectfully submits that the rejections are without appropriate basis and should be withdrawn. In particular, the rejections are not clear as to how Takayanagi and Caldwell are being utilized. Applicant notes that it appears that Caldwell is being utilized to modify Takayanagi; however, the rejection does not clearly make such a modification. In particular, the rejections merely make a naked assertion that it would have been obvious to place tape or film in a capsule for oral administration; however, the rejections do not point to any teaching or suggestion within the prior art to modify Takayanagi in such a manner. The rejections do refer to Caldwell; however, the portion of Caldwell noted in the rejections do not appear to teach or suggest inserting a tape or a film into a capsule.

Expanding upon the above, Applicant notes that Takayanagi is directed to a slow releasing adhesive medical tape for oral mucosa which is a film-form adhesive medicament and the medicament-containing layer of which is at least water-soluble and is gradually dissolved to provide the medical effect. In particular, Takayanagi is directed to an adhesive medical tape for oral mucosa comprising a support layer composed of an intestine-soluble polymer and at least one medicament-containing layer composed of a water-soluble polymer containing at least one kind of an antiphlogistic and analgesic medicament.

The medicament layer of Takayanagi may be composed of one layer but is disclosed to preferably be composed of two or more layers. In the case of two layers, the layer (layer II) adhering to a mucous membrane is composed of a fast dissolving layer and other layer (layer I) is composed of a slow dissolving layer to control the dissolution of the medicament layer or the concentration of the medicament in layer II is increased, whereby the adhesive medical tape having a quick acting property and a long lasting property is obtained.

Takayanagi further discloses that the support layer is composed of such an intestine-soluble polymer to prevent the form of the adhesive medical tape from being collapsed or deformed and also prevent the face (front face) of the adhesive medical tape opposite the face sticking to a mucous membrane from sticking to other mucous membrane.

Still further, Takayanagi discloses at column 4, lines 32-33, that a cover film for protecting the medicament layer can be used, if necessary. However, Takayanagi does not appear to provide any further disclosure of such a cover film and any specific association with the disclosed medical tape. For example, Takayanagi does not teach or suggest that the adhesion site-controlling layer may attach to the protecting layer, as recited in Applicant's claim 1. Moreover, Takayanagi does not teach or suggest that the adhesion site-controlling layer is attached to the protecting layer, as recited in Applicant's claim 22. Still further, Takayanagi does not teach or suggest that the drug-carrying layer is sealed between the adhesion site-controlling layer and the protecting layer to prevent leaking of the drug, as recited in dependent claim 23. Thus, in Applicant's invention, the intermediate drug-carrying layer can be contained in a closed space surrounded by the adhesion site-controlling layer and the protecting layer, and the drug-carrying layer (i.e., the drug) can be prevented from contacting with the outer environment. Owing to such construction, the oral formulation of the present invention can achieve advantageous effects such as good bioavailability. See, for example, page 7, line 13 to page 8, line 3 of the present specification. In contrast, the medical tape of Takayanagi is a simple tape formulation, and the edge of the tape is not processed. Therefore, the medicament is contained in a opened (not closed) space and is contacted with an outer environment at edge portions of the tape.

Still further, Applicant's dependent claim 8 recites that the protecting layer is a film or a capsule made of a water-insoluble polymer or a wax. In this regard, the Examiner's attention is directed to Applicant's specification, at page 11, lines 6-22. Neither Takayanagi nor Caldwell teaches or suggests a protecting layer of water-insoluble polymer.

The rejections attempt to overcome any deficiency in Takayanagi by asserting that one having ordinary skill in the art would have been motivated to prepare a film or tape comprising an active agent in a matrix of polymers and to place that tape or film in a capsule for oral administration. The rejections refer to Caldwell to support the assertion that, "One of ordinary skill in the art would have been motivated to do this to retain a dosage form in the stomach for an extended period of time thereby improving bioavailability of the drug (Caldwell, Co. 3, lines 3-11)." However, one having ordinary skill in the art would not have been motivated to modify Takayanagi based upon Caldwell. Accordingly, it is not seen how the rejections support the placing of the adhesive medical tape into a capsule for oral administration.

In particular, Takayanagi throughout his patent discloses the application of the medical tape to the oral cavity with the dissolution of the film in the oral cavity. For example, attention is directed to Takayanagi column 4, line 34 et seq., for disclosure of application to the oral cavity to directly act to the affected part in the oral cavity to which the film is adhered. Still further, Takayanagi discloses at column 4, lines 48-51, that, "In particular, it is a remarkable effect of this invention that the medical effect can be expected immediately after applying the tape." Certainly, one having ordinary skill in the art would not be motivated to place the medical tape of Takayanagi in a capsule when Takayanagi specifically discloses the advantages of his invention as including application of the

medical tape to the oral cavity with the dissolution of the film in the oral cavity, and that the medical effect is immediate.

For at least the reason stated above, one having ordinary skill in the art would not have been motivated to combine the disclosures of Takayanagi and Caldwell, and any combination thereof would not arrive at Applicant's disclosed and claimed invention.

Still further, Caldwell is directed to a gastric retention device comprising a planar disc-shaped or planar multi-lobed figure prepared from at least one erodible polymer, with the device having the properties of (a) compressible to a size suitable for swallowing; (b) expandable to a size which will prevent passage through the pylorus for a predetermined time; (c) sufficiently resistant to forces by a stomach to prevent passage through a pylorus for a predetermined time; and (d) erodible in the presence of gastric juices so that the device after a predetermined time is no longer able to retain or attain the expanded configuration described (b) and/or resist the forces as described in (c). The improvement of bioavailability disclosed in Caldwell, at column 3, lines 3-11, is associated with the specific structure disclosed in Caldwell. Thus, for the sake of argument, if one having ordinary skill in the art would have been motivated to combine Takayanagi and Caldwell, the instantly claimed invention would not be present. At most, any combination of Takayanagi with Caldwell would, at most, cause modification of Takayanagi to be expandable to a size which will prevent passage through the pylorus for a predetermined time; sufficiently resistant to forces by a stomach to prevent passage through a pylorus for a predetermined time; and erodible in the presence of gastric juices so that the device after a predetermined time is no longer able to retain or attain the expanded configuration and/or resist the forces.

Therefore, the prior art of record does not teach or suggest, as recited in Applicant's independent claim 1, of an oral formulation for gastrointestinal drug delivery which comprises an adhesion site-controlling layer for attaching the formulation to a selected site in the digestive tract, a drug-carrying layer for containing a drug and an adhesive and a protecting layer for protecting the drug in the drug-carrying layer, wherein the drug-carrying layer exists between the protecting layer and the adhesion site-controlling layer, and the adhesion site-controlling layer may attach to the protecting layer. Accordingly, the rejections are without appropriate basis and should be withdrawn.

Uyama is added to the rejection of claim 11 with the mere assertion that Uyama teaches that interferon can be orally administered in various forms, and that one of ordinary skill in the art would have been motivated to place as active agent such as interferon in a film composition that is administered in capsule form to treat various diseases such as retinal edema. However, the question to answer is not whether a drug is a conventional drug, but whether one having ordinary skill in the art would have been motivated to modify Takayanagi to include such a conventional drug in capsule form. Hewlett-Packard Co. v. Bausch & Lomb Inc., 15 USPQ2d 1525 (CAFC 1990). In the instant situation, the rejection improperly does not address this issue.

There is absolutely no convincing line of reasoning present here that would lead one having ordinary skill in the art to incorporate the medical tape of Takayanagi in a capsule. Moreover, Takayanagi discloses medical tapes for oral mucosa including at least one kind of an antiphlogistic and analgesic medicament. The rejection must therefore establish motivation for placing the medical tape of Takayanagi in a capsule and for incorporating interferon as the medicament in the medical tape of Takayanagi. Certainly, the rejection has not provided such motivation when Takayanagi is designed for treatment of oral mucosa and not for delivery of medicaments such as interferon.

Additionally, each of the dependent claims is patentable over the prior art of record in view of the fact that each of these dependent claims includes the limitations of the claims from which they depend. Moreover, each of the dependent claims is patentable over the prior art of record because it would not have been obvious to one having ordinary skill in the art to incorporate such dependent claim features into the invention as more broadly recited in the claims from which they depend.

In view of the fact that a prima facie case of obviousness has not been established for independent claim 1, for the sake of brevity, the specific features of each of these dependent claims is not being individually argued at the present time except for the statement that each of these claims is patentable over the prior art for the combination of features recited therein. However, certain of the features of Applicant's dependent claims will be further discussed below.

The rejections do not address many features of Applicant's dependent claims. Thus, for example, the rejections do not address a three layer laminated formulation, as recited in dependent claim 2 and the thicknesses of the layers, as recited in dependent claim 3.

Still further, the rejections do not address the features of the formulation recited in dependent claim 4 wherein the protecting layer is in hemispherical form forming an inner space and an opening part, and the drug-carrying layer exists in the inner space of the protecting layer in said hemispherical form, and wherein the adhesion site-controlling layer covers the opening part of the protecting layer in said hemispherical form. Still further, the rejections do not address the dimensions recited in dependent claim 5.

Still further, the rejection does not address the ingredient recited in dependent claim 7 or, as discussed above, the protecting layer being a film or a capsule made of a water-insoluble polymer or a wax, as recited in dependent claim 8.

For the Examiner's further understanding of Applicant's invention, Applicant is submitting herewith a copy of a pamphlet, Oral Protein/Peptide Delivery Technology, Ver 1.2, March 1, 2002, "Gastrointestinal Mucoadhesive Patch System (GI-MAPS™), which describes Applicant's invention.

Accordingly, the rejections of record should be withdrawn as improper, and all of the claims should be indicated as allowable.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejection of record, and allow each of the pending claims.

Applicant therefore respectfully requests that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Any amendments to the claims which have been made in this amendment, and which have not been specifically noted to overcome a rejection based upon the prior art, should be considered to have been made for a purpose unrelated to patentability, and no estoppel should be deemed attached thereto.

Should the Examiner have any questions regarding this Response, the this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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APPENDIX
MARKED UP COPY OF CLAIMS 1 AND 4

1. (Amended) An oral formulation for gastrointestinal drug delivery which comprises an adhesion site-controlling layer for attaching the formulation to [the] a selected site in the digestive tract, a drug-carrying layer for containing a drug and an adhesive and a protecting layer for protecting the drug in the drug-carrying layer, wherein the drug-carrying layer exists between the protecting layer and the adhesion site-controlling layer, and the adhesion site-controlling layer may attach to the protecting layer.

4. (Amended) The oral formulation for gastrointestinal drug delivery according to claim 1 wherein the protecting layer is in [the] hemispherical form forming an inner space and an opening part, and the drug-carrying layer exists in the inner space of the protecting layer in said hemispherical form, and wherein the adhesion site-controlling layer covers the opening part of the protecting layer in said hemispherical form.